October 17, 1949.

Dr. Howard B. Newcombe,
Biology Division,
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Chalk River, Ontario, Canada.

Dear Howard:

Just read your last paper in Genetics, and was glad to see at least part of the explanation revealed. However, I still think that nuclear segregation plays about half the part in "delayed mutations". As I think I've mentioned to you in conversation and correspondence, and elsewhere (J. Bact. 56: 695), about half the fermentative mutants recovered after irradiation are as sectors in mixed colonies, rather than as pure mutant clones. This is an especially convenient system, as the mutant sectors can be scored visually.

I am enclosing a rehash I have been using for class purposes of the derivation of the distribution of mutants. By using a somewhat different model (mutations occurring only at fissions, so that they will have precisely one mutant descendant in the first generation next thereafter, you will notice that the rates estimated from r are about twice compared to the rates from p_0, relative to the derivation of L&D. I found also that the development of "d", the mean number of mutants per mutation was a necessary pedagogic step in explaining your spreading experiment in Nature, and your work on phenotypic lag. I think that it should also be pointed out that the pooling of rate estimations by taking their mean is fallacious, and will result in overestimates, unless account is taken of the increase in C over the entire series of experiments. The bias can be very appreciable.

I wonder if you have ever thought of a system where the L&D model, and the one expounded here, might be distinguished, as they could be if it were possible to take account of phenotypic lag, nuclear segregation etc. in estimating "d".

Yours sincerely,

Joshua Lederberg